

ONLINE-ONLY SUPPLEMENTAL MATERIAL

Hemoglobin glycation index, calculated from a single fasting glucose value, as a prediction tool for severe hypoglycemia and major adverse cardiovascular events in DEVOTE

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Supplementary Figure S1 – Baseline HbA_{1c} and FPG in DEVOTE

Supplementary Table S1 – HGI tertile variability in the whole trial population and insulin-naïve participants from baseline to 24 months

Supplementary Table S2 – Comparison of risk of MACE and severe hypoglycemia between baseline HGI risk tertiles over 24 months in the whole trial population and in insulin-naïve participants

Supplementary Table S3 – Time to first occurrence of MACE adjusted for HGI as a time-varying covariate and HGI baseline tertile across the whole trial population

Supplementary Figure S1 – HGI and glycemic parameters

a) Relationship between HbA_{1c} and FPG at baseline in the whole trial population and in insulin-naïve participants

Lines represent the linear regression of HbA_{1c} on FPG: whole trial population, predicted HbA_{1c}=0.0131 FPG [mg/dL] + 6.1751; insulin-naïve participants, predicted HbA_{1c} =0.0156 FPG [mg/dL] + 5.7688

b) Distribution of HGI based on FPG/HbA_{1c} and HGI based on SMBG in the whole trial population at baseline

HGI, HGI based on FPG and HbA_{1c} (model parameters learned at baseline). HGI SMBG, HGI based on SMBG and HbA_{1c} (model parameters learned at month 3).

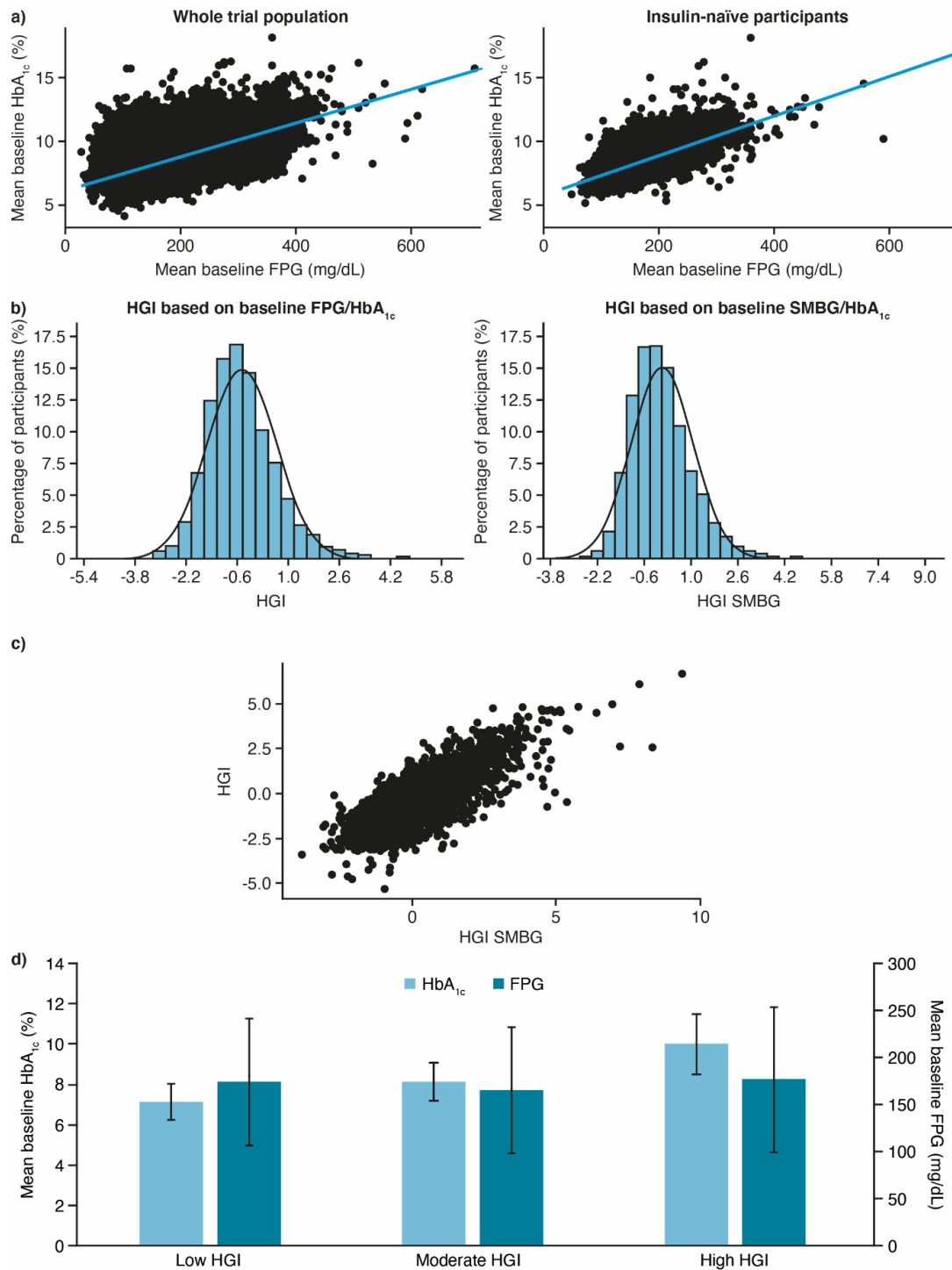
c) Relationship between HGI based on FPG/HbA_{1c} and HGI based on SMBG/HbA_{1c} in the whole trial population at 24 months

HGI, HGI based on FPG and HbA_{1c} (model parameters learned at baseline). HGI SMBG, HGI based on SMBG and HbA_{1c} (model parameters learned at month 3).

d) Distribution of baseline HbA_{1c} (%) and FPG (mg/dL) by baseline HGI tertile in the whole trial population

Data are observed baseline mean ± SD.

FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin; HGI, hemoglobin glycation index; SD, standard deviation; SMBG, self-measured blood glucose.



Supplementary Table S1 – HGI tertile variability in the whole trial population and insulin-naïve participants from baseline to 24 months

	HGI tertile at baseline					
	Whole trial population, n (%)			Insulin-naïve, n (%)		
	Low	Moderate	High	Low	Moderate	High
Low, n (%)						
Baseline	2493 (100)			401 (100)		
12 months	1498 (65.6)	626 (27.4)	160 (7.0)	220 (59.6)	114 (30.9)	35 (9.5)
24 months	1034 (62.1)	474 (28.5)	157 (9.4)	159 (58.7)	88 (32.5)	24 (8.9)
Moderate, n (%)						
Baseline		2498 (100)			403 (100)	
12 months	993 (42.8)	921 (39.7)	406 (17.5)	160 (43.1)	146 (39.4)	65 (17.5)
24 months	666 (40.6)	678 (41.3)	297 (18.1)	117 (42.9)	98 (35.9)	58 (21.2)
High, n (%)						
Baseline			2495 (100)			401 (100)
12 months	576 (25.5)	836 (37.1)	844 (37.4)	121 (33.1)	117 (32.0)	128 (35.0)
24 months	386 (26.2)	554 (37.6)	532 (36.1)	73 (29.6)	86 (34.8)	88 (35.6)

HGI, hemoglobin glycation index; n, number of participants.

Supplementary Table S2 – Time to first occurrence of MACE and severe hypoglycemia between baseline HGI risk tertiles over 24 months in the whole trial population and in insulin-naïve participants

	MACE		Severe hypoglycemia	
	Whole trial population	Insulin-naïve participants	Whole trial population	Insulin-naïve participants
<i>p</i> -value for interaction between HGI tertile and outcome	<0.0001	0.2279	0.0911	0.1668
Low vs Moderate	1.08 [0.89; 1.32]	1.35 [0.78; 2.35]	0.81 [0.64; 1.03]	0.92 [0.42; 2.02]
Low vs High	0.73 [0.61; 0.87]		0.78 [0.61; 0.98]	
Moderate vs High	0.67 [0.56; 0.81]			

Data are Cox's proportional hazard ratios [95% CI] unless otherwise stated. Missing data were not tested.

CI, confidence interval; HGI, hemoglobin glycation index; MACE, major adverse cardiovascular event.

Supplementary Table S3. Time to first occurrence of MACE adjusted for HGI as a time-varying covariate and HGI baseline tertile across the whole trial population

	MACE HR [95% CI]
HGI, Low vs Moderate	0.95 [0.75; 1.19]
High vs Moderate	1.08 [0.84; 1.38]
<i>p</i> -value for interaction between HGI tertile and outcome	0.6361
HGI, baseline Low vs Moderate	1.13 [0.89; 1.43]
High vs Moderate	1.42 [1.12; 1.80]
<i>p</i> -value for interaction between HGI tertile and outcome	0.0152

Hazard ratio is based on Cox regression with treatment and HGI baseline level as factors and HGI as a time-dependent factor. The *p*-value is based on a type 3 test for the factor.

CI, confidence interval; HGI, hemoglobin glycation index; HR, hazard ratio; MACE, major adverse cardiovascular event.